

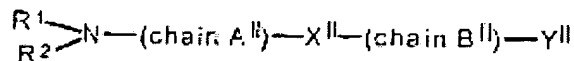


## ATTACHMENT A Amendments to the Claims

*This listing of claims will replace all prior versions, and listings, of claims in the application.*

1-88. (Cancelled)

89. (Currently Amended) A method for treating symptoms associated with cognitive disorders selected from the group consisting of attention, wakefulness and memory disorders ~~Alzheimer disease, attention, wakefulness and/or memorization disorder~~, said method comprising administering in an amount effective to inhibit H<sub>3</sub> receptor activity to a patient in need thereof ~~at~~ the compound having the general formula (IIa)



(IIa)

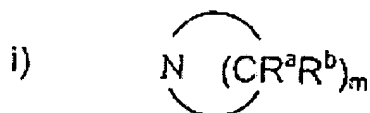
wherein:

R<sup>1</sup> and R<sup>2</sup> may be identical or different and represent each independently a lower alkyl

- ~~a lower alkyl or cycloalkyl,~~

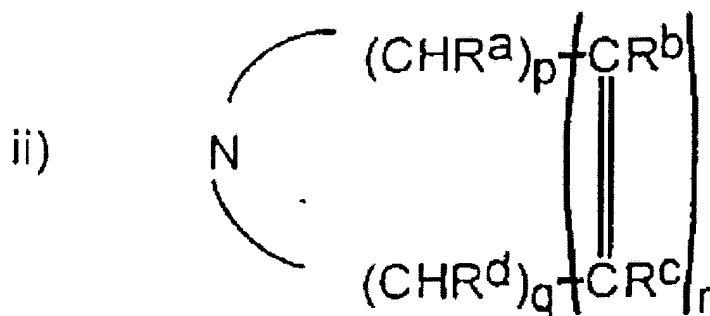
or taken together with the nitrogen atom to which they are attached,

- a saturated nitrogen-containing ring



with m ranging from 2 to 86, or

- a non-aromatic unsaturated nitrogen-containing ring



with p and q being 0 to 3 independently 1 or 2 and r being 1 from 0 to 4, provided that p and q are not simultaneously 0 and  $2 \leq p + q + r \leq 8$ ,

$R^{a-d}$  being independently a hydrogen atom or a lower alkyl, ~~cycloalkyl~~, or carboalkoxy group, or

- a morpholino group, or
- a N-substituted piperazino group:



with R being a lower alkyl, cycloalkyl, carboalkoxy, aryl, arylalkyl, an alkanoyl or aroyl group; and

(i) the chain  $A''$  selected from a saturated ~~or unsaturated~~, straight or branched hydrocarbon chain containing 1 to 6 carbon atoms, the saturated hydrocarbon chain optionally may be interrupted by a hetero atom which may be a sulphur atom;

(ii)  $X''$  selected from an oxygen atom, ~~sulphur atom, -NH-, -NHCO-, -N(alkyl)CO-, NHCONH-, NH-CS-NH-, NHCS-, -O-CO-, CO-O-, -OCONH-, -OCON(alkyl)-, OCON(alkene)-, OCONH-CO-, -CONH-, -CON(alkyl)-, SO-, CO-, -CHOH-, N(saturated or unsaturated alkyl)-, and~~ -S-C(=NY'')-NH-Y''- with the Y'' identical

or different, and  $\text{NR}_{II}\text{C}(=\text{NR}_{II}^I)\text{NR}_{II}^I$  where  $\text{R}_{II}$  AND  $\text{R}_{II}^I$  denote a hydrogen atom or a lower alkyl radical and  $\text{R}_{II}^I$  denotes a hydrogen atom or another powerful electronegative group, which may be selected from a cyano or  $\text{COY}_4^I$  group,  $\text{Y}_4^I$  denoting an alkoxy group;

(iii) the chain  $\text{B}^I$  selected from an aryl; arylalkyl; arylalkanoyl group; a straight alkylene chain  $-(\text{CH}_2)_{n_{II}}-$ ,  $n_{II}$  being an integer which can vary between 1 and 5 or a branched alkylene chain containing from 2 to 8 carbon atoms, the alkylene chain being optionally interrupted by one or a number of oxygen or sulphur atoms; and a group  $-(\text{CH}_2)_{n_{III}}-\text{O}-$  or  $-(\text{CH}_2)_{n_{III}}-\text{S}-$  where  $n_{III}$  is an integer equal to 1 or 2; and

(iv)  $\text{Y}^I$  selected from a straight or branched alkyl group containing 1 to 8 carbon atoms; a cycloalkyl containing 3 to 6 carbon atoms; a bicycloalkyl group; a cycloalkenyl group; an aryl group such as an optionally substituted phenyl group; a 5- or 6-membered heterocyclic radical containing one or two heteroatoms chosen from nitrogen and sulphur atoms, the heterocyclic radical optionally being substituted; and a bicyclic radical resulting from the fusion of a benzene ring to a heterocycle as defined above;

or

(i') the chain  $\text{A}^I$  selected from an unbranched, or branched or unsaturated alkyl group  $-(\text{CH}_2)_{n_{IV}}-$  where  $n_{IV}$  is an integer which can vary between 1 and 8; an unbranched or branched alkene group comprising from 1 to 8 carbon atoms; and an unbranched or branched alkyne group comprising from 1 to 4 carbon atoms;

(ii') the group  $X^{II}$  selected from  $-OCONH-$ ,  $OCON(alkyl)-$ ,  $OCON(alkene)-$ ,  $-OCO-$ ,  $-OCSNH-$ ,  $-CH_2-$ ,  $-O-$ ,  $-OCH_2CO-$ ,  ~~$-S-$ ,  $-CO-$ ,  $-CS-$ , armine,~~ and saturated or unsaturated-alkyl;

(iii') the chain  $B^{II}$  selected from an unbranched, branched or unsaturated lower alkyl comprising from 1 to 8 carbon atoms;  $-(CH_2)_{n_{II}}(hetero\ atom)-$  where the hetero atom is preferably a sulphur or oxygen atom;  $n_{II}$  being an integer which can vary between 1 and 5; and

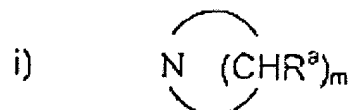
(iv') the group  $Y^{II}$  represents a phenyl group, unsubstituted or mono- or polysubstituted with one or more identical or different substituents selected from halogen atoms,  $OCF_3$ ,  $CHO$ ,  $CF_3$ ,  $SO_2N(alkyl)_2$  such as  $SO_2N(CH_3)_2$ ,  $NO_2$ ,  $S(aryl)$ ,  $SCH_2(phenyl)$ , an unbranched or branched alkene, ~~an unbranched or branched alkyne~~ optionally substituted with a trialkylsilyl radical,  $-O(alkyl)$ ,  $-O(aryl)$ ,  $-CH_2CN$ , a ketone, an aldehyde, a sulphone, an acetal, an alcohol, a lower alkyl,  $-CH=CH-CHO$ ,  $-C(alkyl)=N-OH$ ,  $-C(alkyl)=N-O(alkyl)$  and other keto derivatives,  $-CH=NOH$ ,  $-CH=NO(alkyl)$ , and other aldehyde derivatives,  $-C(alkyl)=NH-NH-CONH_2$ , an O-phenyl or  $-OCH_2(phenyl)$  group,  $-C(cycloalkyl)=NOH$ ,  $-C(cycloalkyl)=N-O(alkyl)$ ; an optionally substituted heterocycle; a cycloalkyl; ~~a bicyclic group and a norbornyl group;~~ a phenyl ring fused to a heterocycle comprising a nitrogen hetero atom or to a carbocycle or a heterocycle bearing a keto function; an unbranched or branched lower alkyl comprising from 1 to 8 carbon atoms; ~~an unbranched or branched alkyne comprising from 1 to 8 carbon atoms;~~ a linear or branched alkyl mono- or polysubstituted with phenyl groups which are either unsubstituted or mono- or polysubstituted; a phenyl alkyl ketone in which the alkyl group is branched or unbranched or cyclic; a substituted or

unsubstituted benzophenone; a substituted or unsubstituted, unbranched or branched or cyclic phenyl alcohol; an unbranched or branched alkene; a piperidyl group; a phenylethyl group; a polycyclic group, in particular a fluorenyl group, a naphthyl or polyhydronaphthyl group or an indanyl group; a phenol group; a ketone or keto derivative; a diphenyl group; a phenoxyphenyl group; a benzyloxyphenyl group, or its pharmaceutically acceptable salts, hydrates, or hydrated salts, or the polymorphic crystalline structures of these compounds or their optical isomers, racemates, diastereoisomers or enantiomers, as a ligand of the histamine H<sub>3</sub>-receptors.

90. (Previously Presented) The method according to claim 89, wherein R<sup>1</sup> and R<sup>2</sup> are independently a lower alkyl group.

91. (Previously Presented) The method according to claim 90, wherein R<sup>1</sup> and R<sup>2</sup> are each an ethyl group.

92. (Previously Presented) The method according to claim 89, wherein -NR<sup>1</sup>R<sup>2</sup> is a saturated nitrogen-containing ring:



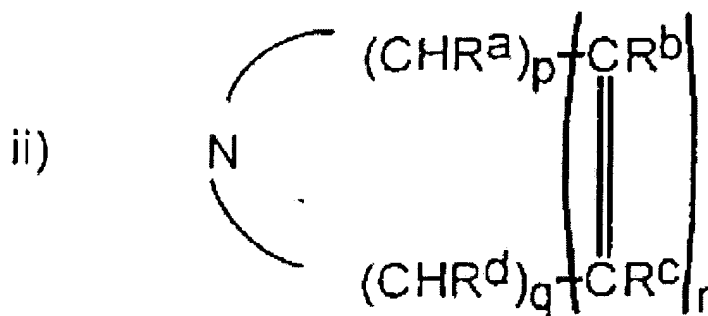
m being as defined in claim 89.

93. (Previously Presented) The method according to claim 92, wherein m is 4, 5 or 6.

94. (Previously Presented) The method according to claim 93, wherein -NR<sup>1</sup>R<sup>2</sup> is a piperidyl group.

95. (Previously Presented) The method according to claim 93, wherein -NR<sup>1</sup>R<sup>2</sup> is a pyrrolidinyl group.

96. (Previously Presented) The method according to claim 89, wherein -NR<sup>1</sup>R<sup>2</sup> is a non-aromatic unsaturated nitrogen-containing ring:



R<sup>a-d</sup> and p, q and r being defined in claim 89.

97. (Canceled).

98. (Previously Presented) The method according to claim 97, wherein p is 2 and q and r are 1.

99. (Previously Presented) The method according to claim 92, wherein R<sup>a-d</sup> are each a hydrogen atom.

100. (Previously Presented) The method according to claim 93, wherein R<sup>a-d</sup> are each a hydrogen atom.

101. (Previously Presented) The method according to claim 94, wherein R<sup>a-d</sup> are each a hydrogen atom.

102. (Previously Presented) The method according to claim 95, wherein R<sup>a-d</sup> are each a hydrogen atom.

103. (Previously Presented) The method according to claim 96, wherein R<sup>a-d</sup> are each a hydrogen atom.

104. (Previously Presented) The method according to claim 97, wherein R<sup>a-d</sup> are each a hydrogen atom.

105. (Previously Presented) The method according to claim 92, wherein the nitrogen-containing ring i) or ii) is one of mono- and di-substituted.

106. (Previously Presented) The method according to claim 105 wherein the nitrogen-containing ring i) or ii) is mono-substituted with an alkyl group.

107. (Previously Presented) The method according to claim 105, wherein the nitrogen-containing ring is mono-substituted with a methyl group.

108. (Previously Presented) The method according to claim 105, wherein the substituent(s) is(are) in beta-position with respect to the nitrogen atom.

109. (Previously Presented) The method according to claim 89, wherein -NR<sup>1</sup>R<sup>2</sup> is a morpholino group.



110. (Previously Presented) The method according to claim 89, wherein -NR<sup>1</sup>R<sup>2</sup> is a N-substituted piperazino group.

111. (Previously Presented) The method according to claim 110, when the piperazino group is N-acetylpiperazino.

112. (Previously Presented) The method according to claim 89, wherein X<sup>II</sup> is selected from -O-, -NH-, -CH<sub>2</sub>-, -OCONH-, -NHCO-, and -NHCONH-.

113. (Previously Presented) The method according to claim 112, wherein X<sup>II</sup> is -O-.

114. (Previously Presented) The method according to claim 89, wherein Y<sup>II</sup> is selected from a linear or branched alkyl group; a cycloalkyl group which may be selected from a particular cyclopentyl and cyclohexyl group; a phenyl group unsubstituted or mono-substituted; a heterocyclic radical; and a bicyclic radical.

115. (Previously Presented) The method according to claim 114, wherein Y<sup>II</sup> comprises a phenyl group unsubstituted or mono-substituted.

116. (Previously Presented) The method according to claim 89, wherein Y<sup>II</sup> represents a phenyl group at least mono-substituted with a keto-substituent which may

include a linear or branched chain aliphatic ketone comprising from 1 to 8 carbon atoms and optionally bearing a hydroxyl group, a cycloalkylketone, an aryl alkyl ketone or arylalkenylketone in which the aryl group is optionally substituted, or a heteroaryl ketone.

117. (Previously Presented) The method according to claim 89, wherein  $Y^{II}$  is a phenyl group at least mono-substituted with -CHO, a ketone, an aldehyde, -CH=CH-CHO, -C(alkyl)=N-OH, -C(alkyl)=N-O(alkyl) and other keto derivatives, -CH=N-OH, -CH=NO(alkyl) and other aldehyde derivatives, -C(cycloalkyl)=NOH, -C(cycloalkyl)=N-O(alkyl).

118. (Previously Presented) The method according to claim 89, wherein chain  $A^{II}$  is a chain  $-(CH_2)_{n_{IV}}-$  with  $n_{IV}$  varying from 1 to 6.

119. (Previously Presented) The method according to claim 118, wherein the chain  $A^{II}$  is  $-(CH_2)-$ .

120. (Previously Presented) The method according to claim 89, wherein the chain  $B^{II}$  is  $-(CH_2)_2-$  or  $-(CH_2)_3-$ .

121. (Previously Presented) The method according to claim 89, wherein X is an oxygen atom, the chain  $A^{II}$  and chain  $B^{II}$  are both  $-(CH_2)_3-$ .

122. (Presently Amended) The method according to claim 89, wherein the compound is selected from:

- 3,3-Dimethylbutyl 3-piperidinopropyl ether
- 3-Phenylpropyl 3-piperidinopropyl ether
- 3-(4-Chlorophenyl)propyl 3-piperidinopropyl ether
- 2-Benzothiazolyl 3-piperidinopropyl ether
- 3-Phenylpropyl 3-(4-methylpiperidino)propyl ether
- 3-Phenylpropyl 3-(3,5-cis-dimethylpiperidino)propyl ether
- 3-Phenylpropyl 3-(3,5-trans-dimethylpiperidino)propyl ether
- 3-Phenylpropyl 3-(3-methylpiperidino)propyl ether
- 3-Phenylpropyl 3-pyrrolidinopropyl ether
- 3-(4-Chlorophenyl)propyl 3-(4-methylpiperidino)propyl ether
- 3-(4-Chlorophenyl) propyl 3-(3,5-cis-dimethyl piperidino)propyl ether
- 3-(4-Chlorophenyl) propyl 3-(3,5-trans-dimethyl piperidino)propyl ether
- 3-Phenylpropyl 3-(N,N-diethylamino)propyl ether
- N-Phenyl-3-piperidinopropyl carbamate
- N-Pentyl-3-piperidinopropyl carbamate
- (S)-(+)-N-[2-(3,3-Dimethyl)butyl]-3-piperidinopropyl carbamate
- 3-Cyclopentyl-N-(3-(1-pyrrolidinyl)propyl)propanamide
- N-Cyclohexyl-N'-(1-pyrrolidinyl-3-propyl)urea
- 2-((2-Piperidinoethyl)amino)benzothiazole
- 5-Piperidinopentylamine
- 2-Nitro-5-(6-piperidinohexyl)pyridine

- 3-Nitro-2-(6-piperidinohexylamino)pyridine
- 2-(6-Piperidinohexylamino)pyrimidine
- N-(6-Phenylhexyl)piperidine
- N-phenyl-N'-(diethylamino-3-propyl)urea
- N-benzyl-N'-(3-piperidinopropyl)guanidine
- N-(3-(N,N-Diethylamino)propyl)N'-phenylurea
- N-Cyclohexylmethyl-N'-(3-piperidinopropyl)guanidine, or its

pharmaceutically acceptable salts, hydrates, or hydrated salts, or the polymorphic crystalline structures of these compounds or their optical isomers, racemates, ~~racemates~~ diastereomers ~~diastereoisomers~~ or enantiomers.

123. (Canceled)

124. (Previously Presented) The method of treatment according to Claim 89 wherein the heterocycle comprises a sulphur hetero atom.

125-127. (Canceled)

128. (Currently Amended) The method of treatment according to claim 89, wherein the symptoms ~~Alzheimer disease, attention, wakefulness and/or memorization disorders~~ occur in an aged person.

129-153. (Canceled)

154. (Previously presented) The method according to claim 89 wherein said compound is 3-(4-chlorophenyl)propyl-3-piperidinopropylether or its pharmaceutically acceptable salts, hydrates, or hydrated salts, or the polymorphic crystalline structures of these compounds or their optical isomers, racemates, diastereoisomers or enantiomers.

155. (Previously presented) The method according to claim 153 wherein said compound is in the form of a pharmaceutically acceptable salt chosen from the group consisting in hydrochloride, hydrobromide, hydrogen maleate, hydrogen oxalate.

156. (New) The method according to claim 89 wherein said cognitive disorder is Alzheimer's disease.

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